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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,171	07/01/2003	Carol A. Tosaya	D-02017A	5208

7590 11/24/2008

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EXAMINER	
KISH, JAMES M	

ART UNIT	PAPER NUMBER
3737	

MAIL DATE	DELIVERY MODE
11/24/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/612,171	TOSAYA ET AL.	
	Examiner	Art Unit	
	JAMES KISH	3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-67,69-79,81-86 and 88-96* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-67,69-79,81-86 and 88-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Allowable Subject Matter

The indicated allowability of claims 45, 46 and 61 is withdrawn in view of the newly discovered reference(s) to Gervais et al. (US Patent Pub. No. 2002/0115717). Rejections based on the newly cited reference(s) follow.

Response to Arguments

Applicant's arguments, filed August 25, 2008, with respect to the prior art reference to Wallace have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made. The following rebuttal is provided with regard to the arguments against Bystritsky.

As previously stated, Bystritsky discloses a method for modifying electrical currents in brain circuits through the simultaneous use of focused ultrasound pulse (FUP). Among other disorders this can be used for are Parkinsonian Disease, Huntington Chorea, La Touretts and tick syndromes. The FUP can be focused to any location(s) in the brain. Long-term changes in the circuitry can be induced. This is described at page 5 of the Office Action dated May 30, 2008. Therefore, Bystritsky teaches and is capable of indirectly (and capable of directly) coupling acoustical energy to a brain or neurological region which has been, is or *is expected to potentially* be subject to the nucleation, growth or deposition of abnormal protein or prion-related deposits, nodules or bodies. This process therefore will, at least, aid in the recovery or

improved chemical, physical or cognitive functionality of brain-related or neurological-related physiology or functional pathways negatively impacted or stressed by the *expected* deposition of, formation of, or presence of said deposits, nodules or bodies. Therefore, Bystritsky reads on the claims.

Regarding the Applicant's arguments that Bystritsky requires simultaneous imaging while the Applicant's invention does not require such a step is irrelevant. Just because Bystritsky has more structure than the claimed invention does not mean that it does not have the claimed subject matter.

Applicant's argue that the claimed invention does not *require* functional imaging while Bystritsky does require such imaging methods. This is irrelevant because claim 22 clearly claims that one option (among many) is, at least, fMRI and PET, which are *both* functional imaging methods.

On page 33, Applicant states, "while the Applicant's targets are undesirable electrically inactive plaques." The Examiner respectfully disagrees. The claim states, "…coupling, directly or indirectly, acoustic or vibratory emissions into a brain or neurological region which has been, is, or is *expected to potentially* be subject to the… growth… of abnormal-protein or prion-related… bodies." First of all, the region is not well defined and may include the entire brain as the region where such abnormal-protein or prion-related bodies (not plaque) may be *expected to potentially* form. Secondly, the abnormal-protein or prion-related bodies may not even be there yet, or they may have already "disappeared." Thirdly, the emissions may be indirectly coupled to the region, therefore, they may be directed to some other area of the body that will

create an effect in the *region* where the abnormal-protein or prion-related bodies (not plaque) may be *expected to potentially* form. Therefore, the Applicant's target of the emissions of acoustic or vibratory energy are not plaque.

Regarding the Applicant's argument that there is no disclosure of suggestion in Bystritsky that abnormalities in Cortico-Talamic-Straitum Circuit (which is discussed in connection with Parkinsonian Disease – as stated by the Applicant on page 33) involve abnormal-protein or prion-related bodies: Claim 27 of the current invention clearly states that Parkinson's Disease is one of many abnormal-protein or prion-related diseases that may be treated. Therefore, it is common knowledge to those of skill in the art that a circuit in the brain or neurological *region* that is associated with symptoms of such an abnormal-protein or prion-related disease, such as Parkinson's Disease, would be a " region which has been, is, or is *expected to potentially* be subject to the… growth… of abnormal-protein or prion-related… bodies."

For at least the reasons stated above, Bystritsky still reads on the claimed invention.

The Wallace references has been removed from the rejections, however, the Examiner will respond nonetheless to illustrate how Wallace in fact, reads on the claims.

Wallace in combination with Shalev teach any one of electrical, vibrational or ultrasonic stimulation of a *region* of the brain in order to treat Alzhemier's disease. The fact that "this is a preventative measure as well, as opposed to a reversal of an existing deposition (Remarks, page 36)" is irrelevant because the claims clearly state, "coupling … emissions into a... region which... is expected to potentially be subject to the...

growth... of... bodies." This *clearly* states preventative measures. The fact that not *all* of the many options provided by the claims is disclosed or suggested by a reference is irrelevant. If *any* of the possibilities is disclosed, it reads on the reference.

The fact that Wallace's field or energy is no "***directly*** acting upon a deposition (page 36)" is irrelevant because the emissions, as claimed, are aimed at a *region* which has been or is expected to pottntially be subject to a deposition. Therefore, the claims do not state that the energy is applied to a deposit.

Regarding the argument that Wallace is "***not*** applied directly to neurally damaged tissue but are even indirectly applied to his first portion of tissue as well" merely means that Wallace is indirectly applying energy to a *region* which has been or is expected to pottntially be subject to a deposition, i.e., the brain. This is covered by the claims because they state, "indirectly."

Regarding the argument on page 36 that "No method... that indirectly increases blood flow in a neurally diseased region will lead one skilled in the this art to Applicants' method," the Examiner respectfully disagrees. The Applicant is reminded that the only method claims in the application are claims 86 and 95. As described above, Wallace in combination with Shalev teaches acoustically coupling [a] patient's brain to acoustic therapy means comprising at least one acoustic or vibration emitter for acoustically or mechanically coupling, … indirectly,… emissions into a brain region (i.e., the brain) which has been, is, or is expected to potentially be subject to the… growth… of… bodies; exciting said emitter...; delivering therapeutic acoustic or vibration energy... indirectly, to at least one said brain... region, therapy *designed to* provide, enable… at

least one of the following therapy processes: (ii) interference in, slowing of… at least one physical, chemical, biological or genetic… body formation-process; (iii)improved cognitive functionality of brain-related... functional pathways negatively impacted or stressed by the… presence of… bodies," with the option of a drug.

On the top of page 29, the Applicant states, “claims 30 and 32 positively recite the use of these items [the drug, medicament or controlled dietary matter or content]. The Examiner respectfully disagrees. Much in the same way that claim 34 recites two alternatives (i.e., aided or unaided), wherein when "in aided form, then options (a), (b), (c), or (d) may be employed;” claim 1 recites two alternatives (i.e., with a drug or without a drug). Claim 30 then provides that when chosen "with a drug," at least one of said drug… is either (a) or (b). Therefore, claims 30 and 32 do not positively require the drug, but provide more options if it is chosen. Regarding claim 44, this states that “said acoustic or vibratory exposure… *enables*… to a *useful degree* the rate or extent of a least one said breakup, interference or aiding process via *mainly* acoustic-driven mechanisms without the required use of” the drugs. Therefore, the Examiner agrees that the drug is positively not included in claim 44. However, this claim does not state that the exposure definitely provides any affect (see the following paragraph regarding this argument). Furthermore, "a useful degree" is subjective to interpretation is nondescript. Still, "mainly" implies that it is not entirely provided by the acoustic-driven mechanisms and allows for another substance, i.e., increased blood flow to the region, to provide assistance in the breakup, interference or aiding process.

The Examiner would like to address the Applicant's arguments on page 29 of the Remarks filed on December 5, 2007, as they are relevant to the following rejection. The Applicant argues on page 29, lines 18-20, "there is no disclosure or suggestion that the targeted region of the brain itself is exposed to ultrasound and the optional drug to thereby enhance the ***effect of the therapeutic treatment*** over ultrasound alone." The Examiner respectfully finds this argument to contain error based on the interpretation that the ultrasound need not be required to positively induce an effect alone, as interpreted by the claims. Meaning, the claims (for example, claim 1) reads, "the [acoustic exposure] therapy designed to… enable… at least one of the following therapy processes… wherein said acoustic or vibration energy is capable of… enabling… said acoustic or vibratory therapy process… employing a drug, medicament, vitamin, mineral or controlled dietary matter or content." Therefore, one *of many* possible interpretations is that the emissions *enable* the therapy by employing the drug. To enable means "to make possible (Merriam-Webster)." Therefore, the claim teaches that the emissions make it *possible* to provide therapy. However, they do not require it to provide therapy. Therefore, in one interpretation, the claims do not provide therapy and have no patentable utility.

Based on the above paragraph, the Examiner is re-introducing prior art that had previously been applied in the Office Action dated September 5, 2007.

The Examiner notes that, with the exception of claims 86 and 95, all of the claims of the current invention are apparatus/system claims. Section 2113 of the MPEP states, "A claim containing a "recitation with respect to the manner in which a claimed apparatus is intended to be employed does not differentiate the claimed apparatus from a prior art apparatus" if the prior art apparatus teaches all the structural limitations of the claim. Ex parte Masham, 2 USPQ2d 1647 (Bd. Pat. App. & Inter. 1987)." Section 2114 of the MPEP states, "While features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function. In re Schreiber, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997)." Section 2114 of the MPEP states (with emphasis in the original), "'Apparatus claims cover what a device *is*, not what a device *does*.' Hewlett-Packard Co. v. Bausch & Lomb Inc., 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990)."

Therefore, the only portion of, for instance, claim 1 that corresponds to what the system *is*, as opposed to what the system *does*, is "at least one acoustic or vibration emitter… means for exciting said emitter." The remainder of claim 1 does not define what the system *is*. Therefore, any device that teaches an ultrasound transducer that is capable of emitting ultrasound energy (which would therefore inherently have a means for exciting the transducer) reads on independent claim 1.

Another way of stating what is discussed above in the citations of the MPEP is: An apparatus is to be examined (and preferably claimed in a similar manner) as if it were placed in front of the Examiner. If the system requires an MRI to provide an image

of a patient's brain in order to choose a therapy session (as stated in claims 21-22), this is not the system. The system is the apparatus that would be placed in front of the Examiner. Similarly, lab-tests (claim 25) are not the system.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-96 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4, 6-17, and 20-99 of U.S. Patent Application No. 2005/0020945. Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions disclose opening of a blood brain barrier to allow transference of compounds, whether it be CSF or a treatment agent, through the barrier using a similar, if not identical, apparatus.

Claim Objections

Claims 1-67, 69-79, 81-85 and 96 are objected to because of the following informalities:

Claim 1 is objected to for improperly attempting to invoke 112, 6th paragraph on line 4 by stating, "(a) acoustic exposure therapy means comprising…"

Claim 20 is objected to because "sufficiently" in unclear and indefinite. A house is sufficiently portable in that it may be on the back of a large truck on a highway with "wide load" vehicles ahead and behind it. Furthermore, the options (a)-(h) do not further limit the system and are intended use.

Claims 30-31, 35-36, 41, 44-45, 64, 67, 73-74, 81 and 85 are objected to because "said acoustic or vibratory exposure" lacks antecedent basis.

Claims 45 are objected to for failing to remain consistent. Claim 45 states in line 5, "said plaque, fibril, nodule or defect." In line 4, "a plaque, fibril or prion-related deposit or defect" is stated. However, it can only be assumed that "said nodule" refers back to claim 1. It is unclear where the scope of the citation from line 5 lies.

Claims 21-30, 35-36, 61-69, 81-83 and 85 are objected to for failing to further limit the structure of the claims from which they depend. These claims are intended use claims. These claims do not have patentable weight with regard to the system.

In claim 57, there is not sufficient structure to allow for the functions of "diagnostically prob[ing] or measur[ing] a characteristic of the brain, skull, neurological system, disease state, physiological or temperature of said patient or operation of an

emitter…" because the only structure set forth is an emitter. In order to probe or measure, there must be a structure capable of measuring, sensing, detecting, etc.

In claim 60, "said acoustic or vibratory coupling means" lacks antecedent basis.

Claim 65 is objected to because "a beneficial action" is a subjective term and not clearly defining what action is occurring, meant to occur, hoped to occur, preferred to occur, yearned for, expected, wished, aspired, intended, desired, or wanted to have occur to a brain or neurological region that has been, is or is expected to potentially be subject to the nucleation, growth or deposition of abnormal protein or prion-related deposits, nodules or bodies.

In claim 72, several of the options include the phrase, "the helmet or headgear." These lack antecedent basis if "a helmet or headgear" has not been previously described in that particular option. Similarly, option (n) states, "the headgear, helmet or *pillow* structure…" This lacks antecedent basis and is the first mentioning of a pillow structure in the claims. Please review the remaining options for remaining antecedent basis issues.

Further regard to claim 72, option (s) defines a portable or semiportable system. It is unclear if this is referring to the system of claim 1 or some entirely different system.

Even furthermore, claim 72 is objected to because the many options are not related in the least. For example, option (f) discusses acoustic subelements of an emitter, (k) discusses material of a headgear, option (q) discusses patient positioning, option (s) discusses a portable system, option (y) discusses thermal control.

Claims 82-83 is objected for claiming *speculation* that an improvement has occurred based on a process, which the Examiner notes is not the system.

Claim 85 is objected to because it is unclear what "or by said exposure" is referring to in the phrase, "at least one said acoustic or vibratory exposure *or by said exposure*…"

Claim 88 is objected to for improperly invoking 112, 6th paragraph. Furthermore, claim 88 is objected to for failing to positively provide any structure for the system.

In claim 93, there is not sufficient structure to allow for the functions of acoustic measurements or imaging is practiced…" because the only structure set forth is in claim 88 as a means to direct acoustic or vibrational energy, which the Examiner notes, does not define any structure.

Claim 96 is objected to because it is states, "A system for... said method comprising." Each claim must be positively claiming either an apparatus or a method.

Appropriate correction is required.

Again, the Examiner urges that the Applicant thoroughly review the claims for any remaining antecedent basis issues (or any other objectionable problems) that the Examiner may have accidentally overlooked to place the claims in clear and proper form.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 95 is rejected under 35 USC 101 as being directed to non-statutory subject matter because these are method or process claims that do not transform underlying subject matter (such as an article or materials) to a different state or thing, nor are they tied to another statutory class (such as a particular machine). *See* Diamond v. Diehr, 450 U.S. 175, 184 (1981) (quoting *Benson*, 409 U.S. at 70); *Parker v. Flook*, 437 U.S. 584, 588 n.9 (1978) (citing *Cochrane v. Deener*, 94 U.S. 780, 787-88 (1876)). *See also In re Comiskey*, 499 F.3d 1365, 1376 (Fed. Cir. 2007) (request for rehearing *en banc* pending). The method steps provided are "administration of acoustic or vibrational energy into affected or potentially affected patient anatomy portions, said energy altering, blocking or reversing a cognitively-damaging deposition process, at least temporarily." Vibrational energy may be applied by violently shaking a patient, thereby altering a cognitively-damaging deposition process.

Claims 1-4, 7-67, 69-79 and 81-86 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The emission need not be required to positively induce an effect alone, as interpreted by the claims. Meaning, the claims (for example, claim 1) reads, "the [acoustic exposure] therapy designed to… enable… at least one of the following therapy processes… wherein said acoustic or vibration energy is capable of… enabling… said acoustic or vibratory therapy process… employing a drug, medicament, vitamin, mineral or controlled dietary matter or content." Therefore, one *of many* possible interpretations is that the emissions *enable* the therapy by

employing the drug. To enable means "to make possible (Merriam-Webster)." Therefore, the claim teaches that the emissions make it *possible* to provide therapy. However, they do not require it to provide therapy. When this interpretation is combined with the option to not use a drug, the therapy is enabled, but not necessary affecting anything. Therefore, in one interpretation, the claims do not provide therapy and have no industrial applicability.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 11-12, 27-32, 35, 37, 39-42, 45-46, 56-58, 61-67, 69, 72-73, 79, 82-83, 86, 88-90, 92-93, 95-96 are rejected under 35 U.S.C. 102(e) as being anticipated by Gervais et al. (US Patent Pub. No. 200/0115717). Gervais discloses an amyloid targeting molecule-chelator conjugates for imaging, e.g., amyloid plaques in vivo, and/or for the treatment of amyloidosis disorders. The agents (which are able to be injected) are capable of binding specifically to amyloid plaques, as an aid in diagnosis and/or early treatment of amyloidosis disorders (*see* Abstract). In addition to a pulsed method, continuous wave ultrasound such as Power Doppler may be applied. The relatively higher energy of the Power Doppler may be made to resonate the vesicles [carrying an

agent] and thereby promote their rupture. In addition, the process of vesicle rupture may be employed to transfer kinetic energy to the surface, for example of a plaque, to promote amyloid plaque lysis. Thus, therapeutic plaque lysis may be achieved during a combination diagnostic and therapeutic ultrasound (paragraph 187). It is also believed that the amyloid-targeting moiety also prevents the amyloid protein from binding or adhering to a cell surface (paragraph 193). See paragraphs 187 through 193. Also, paragraph 12 states that the agents may be used in the brain.

Regarding claim 12, it is inherent that an ultrasound emitter is either, at least, one of focused or unfocused. Therefore, claim 12 includes all emitters and fails to limit the device.

Regarding claim 56, it is inherent that an operator would set-up such a system based on "(s) changes in locations or concentrations of plaque, fibrils or nodules… from patient to patient."

Regarding claim 69, it is inherent that the any patient undergoing any procedure will (b) receive one… of any one… of said [whatever therapy or procedure is being performed]... over a period of one... sessions.

Regarding claim 72, it is inherent that the patient would necessarily have to receive this treatment at at least one of the optional locations stated in (t). Also, option (u) is provided by Gervais.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 11-16, 20-27, 30-32, 37-38, 44, 50-53, 56, 58, 60, 66, 71-73, 76, 78-79, 84, 86, 88-93 and 95-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bystritsky (US Patent No. 7,283,861) alone. Bystritsky discloses a method for modifying electrical currents in brain circuits through the simultaneous use of focused ultrasound pulse (FUP) and existing brain imaging systems. The methods are used for research, treatment and diagnosis of neurological disorders whose biological mechanisms include brain circuits (*see* Abstract). Among other disorders this can be used for are Parkinsonian Disease, Huntington Chorea, La Touretts and tick syndromes (column 1, lines 25-45). The FUP can be focused to any location(s) in the brain and can account for bone density and structure of the skill and brain (column 4, lines 25-34). Repeated use of the methods disclosed by Bystritsky can cause long-term or permanent changes to the circuits (column 4, lines 45-59). This can be used to aid in the recovery, growth, regrowth, new growth or improved physical, biological and cognitive functionality of brain-related or neurological-related cells, or functional pathways negatively impacted or stressed by deposits, nodules or bodies. The methods may be used without additional agents, but may also be used concurrently with pharmaceutical agents (column 5, lines 21-32). It would have been obvious to one of skill in the art to use these methods on pathways that were adversely effected by

protein formation due to neurological disorders because the methods are specifically cited as a treatment for such diseases (i.e., Parkinsonian Disease, Huntington Chorea, etc.).

Regarding claims 24-26, these claims are method steps claim and do not limit the structure from which these claims ultimately dependent.

Regarding claim 31, the fact that acoustic or vibratory therapy exposure effects the action of the drug is not a structural limitation, but rather is a property based on the drug, medicament, vitamin, etc., that is given to the patient. Bystritsky is capable of enhancing the effects of certain drug, medicament, vitamin, etc., that would be given to the patient if the drugs are effected by ultrasound.

Regarding claim 60, if a patient is bald and the procedure of Bytritsky is performed, a patient with reduced hair quantity will have the device coupled.

Regarding claims 1, 30-43, 49 and 81, the system is claimed to function without the use of a drug, medicament, or controlled dietary content to proceed at a useful pace or to a useful extent. Therefore, the use of a drug, medicament, or controlled dietary content is optional. Since this is not necessary for the system, Bystritsky's methods and system cover these optional limitations.

Regarding claims 88-90 and 92, section (a) is the only portion of the claim that recites positive claim limitations. Section (b) is optional. The two "wherein" clauses following section (b) are intended use limitations. Therefore, the portion of claim 88 that bears patentable weight is limited to section (a), which Bystritsky reads on.

Claims 1-6, 11-16, 21-36, 39-42, 49-56, 58, 60, 62-66, 69, 71-76, 78-79, 81-86, 88-90 and 92-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jolesz et al. (US Patent No. 5,752,515) – herein referred to as Jolesz - in view of Chalifour et al. (US Patent App. 2004/0006092) – herein referred to as Chalifour. Jolesz discloses a method and apparatus for treating neurological disorders by ultrasonic delivery of compounds through the blood-brain barrier (BBB). See column 3, lines 44-67. The ultrasound is applied through the skull itself via a phased array of transducers, a focused ultrasound transducer or a combination of ultrasound source and an acoustic lens, placed outside the skull (column 2, line 66 through column 3, line 37). The ultrasound can be focused electronically or mechanically (column 5, lines 33-41). Discussion of cavitation can be found throughout the reference, and particularly at column 5, line 64 through column 6, line 27. The invention allows for both continuous wave or burst (pulsed) mode operation (column 6, line 24). The device uses image-based localization of the region. Such images can be obtained on the devices described at column 6, lines 38-61. The effects of the skull bone are incorporated to allow the ultrasound to focus at a common location (column 7, lines 33-51). Jolesz does not explicitly state that one such disease to be treated is Alzheimer's or any other protein-related disease, however, Alzheimer's Disease (AD) is a neurological, mental and behavioral disorder, and a known protein-related disease and therefore is incorporated into the possible disorders that are treatable by Jolesz as disclosed at column 3, lines 60-67). Chalifour teaches a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an

amidine compound. The compound is used to, among other things, at least prevent, slow or stop deterioration of cognitive function in a patient (paragraph 75). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate the compounds of Chalifour into the method and system of Jolesz to treat amyloid-related diseases. Furthermore, Chalifour teaches several methods to pass the compound through the BBB and it would be obvious to one of skill in the art to combine the teaches of Chalifour and Jolesz in order to provide a more accurate entry port for the compound through the barrier.

With respect to the specific limitation of the independent claims, Jolesz provides an ultrasound emitter that will provide acoustic energy to a localized portion of the BBB. Therefore, the energy will indirectly enter the brain or neurological region which has been, is or is expected to potentially be subject to the abnormal bodies. The ultrasound will be emitted with a desired characteristic, i.e. in a controlled manner. The compound of Chalifour will then at least prevent, slow or stop deterioration of cognitive function in a patient.

Claims 1, 7-10, 17-20, 41, 43, 59, 61, 77, 88 and 91 rejected under 35 U.S.C. 103(a) as being unpatentable over Brisken et al. (US Patent No. 6,464,680) – herein referred to as Brisken - in view of Chalifour. Brisken discloses a method of enhancing cellular absorption of a substance delivered into a target region with the use of vibrational energy to the target region (see Abstract). The invention can be used in treatment of abnormalities of the brain (column 12, lines 4-14) by allowing treatment to

brain cells protected by the blood-brain barrier (column 1, lines 54-55). In one embodiment, an injection needle and the ultrasound energy emitter are located on the end of a catheter and can be introduced through a blood vessel or other luminal cavity (column 3, lines 4-28). The ultrasound conditions induce a preferred cellular response that increases porosity and subsequent uptake of therapeutic agents (column 5, line 55 through column 6, line 8). See column 7, lines 43-55 for possible effects of drugs. The wave may be divergent or focused on a small spot with the resolution of the ultrasonic emitter device (column 9, lines 65-67 and column 11, lines 54-63). Column 5, lines 38-54 discuss the thermal index of the vasculature immediately around the device. It is monitored based on the equation found at line 43. Chalifour teaches a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. The compound is used to, among other things, at least prevent, slow or stop deterioration of cognitive function in a patient (paragraph 75). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate the compounds of Chalifour into the method and system of Brisken to treat amyloid-related diseases. Furthermore, Chalifour teaches several methods to pass the compound through the BBB and it would be obvious to one of skill in the art to combine the teaches of Chalifour and Brisken in order to provide a more accurate entry port for the compound through the barrier.

Claims 37-38, 57 and 92 rejected under 35 U.S.C. 103(a) as being unpatentable over Jolesz et al in view of Hynynen et al (US Patent No. 6,514,221) – herein referred to

as Hynynen, further in view of Chalifour. Jolesz discloses a method and apparatus for treating neurological disorders by ultrasonic delivery of compounds through the blood-brain barrier (BBB). However, while cavitation is discussed by Jolesz, the compounds delivered through the BBB are not explicitly cavitation aiding agents. Hynynen teaches a method of opening the blood-organ barrier of a subject providing an exogenous agent (see Abstract). The agent is described as having microbubbles or solid particles contained within that will vaporize via body heat or ultrasonic energy (see all of column 5, as well as column 6, lines 1-43). There is also a measure of the temperature elevation due to the sonication (column 9, line 65 through column 10, line 12). Hynynen also discusses non-focused ultrasound at column 10, lines 36-57. It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate a cavitation inducing contrast agent as taught by Hynynen into the system of Jolesz in order to allow opening of the BBB at low enough energy levels so as not to induce thermal damage (see Abstract).

Chalifour teaches a method of treating or preventing an amyloid-related disease in a subject comprising administering to the subject a therapeutic amount of an amidine compound. The compound is used to, among other things, at least prevent, slow or stop deterioration of cognitive function in a patient (paragraph 75). It would have been obvious to one having ordinary skill in the art at the time the invention was made to incorporate the compounds of Chalifour into the method and system of Jolesz to treat amyloid-related diseases. Furthermore, Chalifour teaches several methods to pass the compound through the BBB and it would be obvious to one of skill in the art to combine

the teaches of Chalifour and Jolesz in order to provide a more accurate entry port for the compound through the barrier.

Claims 1-6, 11-16, 21-42, 49-58, 60, 62-66, 69, 71-76, 78-79, 81-86, 88-90 and 92-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Solomon et al. (US Patent Pub. No. 2002/0052311) – herein referred to as Solomon - in view of Schenk (Int. Pub. No. WO 99/27944), further in view of any of Jolesz and Hynynen. Solomon discloses that Schenk teaches administration of beta-amyloid immunogens to a patient in order to generate antibodies to prevent formation of plaques or dissolve exiting plaques. However, Schenk disregards the blood brain barrier which, under normal circumstances, prevents the penetration of antibodies into the brain.

Jolesz discloses a method and apparatus for treating neurological disorders by ultrasonic delivery of compounds through the blood-brain barrier (BBB). See column 3, lines 44-67. The ultrasound is applied through the skull itself via a phased array of transducers, a focused ultrasound transducer or a combination of ultrasound source and an acoustic lens, placed outside the skull (column 2, line 66 through column 3, line 37).

Hynynen teaches a method of opening the blood-organ barrier of a subject providing an exogenous agent (see Abstract). The agent is described as having microbubbles or solid particles contained within that will vaporize via body heat or ultrasonic energy (see all of column 5, as well as column 6, lines 1-43). There is also a measure of the temperature elevation due to the sonication (column 9, line 65 through

column 10, line 12). Hynynen also discusses non-focused ultrasound at column 10, lines 36-57.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the methods of any one of Jolesz and Hynynen in order to open the blood-brain-barrier, which is taught as a deficiency of Schenk in the specification of Solomon, in order to utilize the system and methods of Schenk to its fullest extent.

Claims 1, 7-10, 17-20, 41, 43, 59, 77, 88 and 91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Solomon in view of Schenk, and further in view of Brisken. Solomon discloses that Schenk teaches administration of beta-amyloid immunogens to a patient in order to generate antibodies to prevent formation of plaques or dissolve exiting plaques. However, Schenk disregards the blood brain barrier which, under normal circumstances, prevents the penetration of antibodies into the brain.

Brisken discloses a method of enhancing cellular absorption of a substance delivered into a target region with the use of vibrational energy to the target region (see Abstract). The invention can be used in treatment of abnormalities of the brain (column 12, lines 4-14) by allowing treatment to brain cells protected by the blood-brain barrier (column 1, lines 54-55).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the methods of any one of Brisken in order to open the

blood-brain-barrier, which is taught as a deficiency of Schenk in the specification of Solomon, in order to utilize the system and methods of Schenk to its fullest extent.

Claims 1, 7-10, 17-19, 27-29, 30, 33-36, 39-43, 47-49, 57, 59, 62-67, 69-70, 73-74, 77, 79, 81-83, 85-86, 88-90 and 94-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Solomon in view of Schenk, and further in view of Shalev (US Patent Pub. No. 2003/0176892). Solomon discloses that Schenk teaches administration of beta-amyloid immunogens to a patient in order to generate antibodies to prevent formation of plaques or dissolve exiting plaques. However, Schenk disregards the blood brain barrier which, under normal circumstances, prevents the penetration of antibodies into the brain.

Shalev teaches a method and apparatus for stimulating the sphenopalatine ganglion to modify properties of the blood-brain barrier (BBB) and cerebral blood flow (paragraphs 36-41). Also provided at paragraph 43, Shalev states that the invention provides improved methods for treating neurological diseases (for example, Alzheimer's disease). Methods of stimulation are described as electrical, however, mechanical vibration and ultrasonic transmission are both contemplated (paragraph 68). A temperature transducer is used to monitor the effect of the stimulation applied (paragraph 156).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the methods of any one of Shalev in order to open the

blood-brain-barrier, which is taught as a deficiency of Schenk in the specification of Solomon, in order to utilize the system and methods of Schenk to its fullest extent.

Regarding claims 40 and 41, these claims are purely functional and do not provide patentable limitations for the system.

Regarding claims 35-36, 62-69, 81-83 and 85 are all intended use claims. These claims do not have patentable weight with regard to the system. Solomon in view of Schenk and Shalev cover these limitations.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES KISH whose telephone number is (571)272-5554. The examiner can normally be reached on 8:30 - 5:00 ~ Mon. - Fri..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Casler can be reached on 571-272-4956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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JMK